Paper No. 61

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte RICHARD L. JARVEST
and MICHAEL R. HARNDEN

Appeal No. 2000-0599[1]
Application No. 08/357,363[2]

HEARD: November 29, 2001

---

[1] We note that this appeal is related to an appeal in application serial no. 08/311,291 (Appeal No. 2000-0591). We have considered both appeals together.

[2] Application for patent filed December 15, 1994. According to appellants, this application is a continuation of application serial no. 07/847,833, filed March 9, 1992, now abandoned; which is a continuation of application serial no. 07/697,853, filed May 9, 1991, now abandoned; which is a continuation of application serial no. 07/085,216, filed August 12, 1987, now U.S. Patent No. 5,075,445; which is a continuation of application serial no. 06/641,300, filed August 16, 1984, now abandoned.

Before WILLIAM F. SMITH, SCHEINER and ADAMS, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 30, 32, 33, 45, 46, 48 and 59-61. Claims 49, 51, 57 and 58, also pending in the application, have been allowed by the examiner. The claims on appeal read as follows:

30. 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine having a purity of greater than 95% by weight.

32. 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine having an ultraviolet spectroscopic molar extinction coefficient (ε) of about 11,500 in water at a λ_{max} of about 253 nm.

33. 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine having an ^{1}H-NMR spectrum of d_H [$(CD_3)_2SO$] 1.3-1.5 (3H, m, $CHCH_2CH_2$), 3.42 (4H, d, J 5Hz, 2x CH_2O), 3.99 (2H, t, J 7Hz, CH_2N), 4.41 (2H, br, D_2O exchangeable, 2x OH), 6.44 (2H, s, D_2O exchangeable, 2-NH_2), 7.71 (1H, s, 8-H), and 10.55 (1H, br, D_2O exchangeable, 1-H), and having substantially no detectable signal in the δ7.1-7.4 region of the ^{1}H-NMR spectrum.

45. 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine in substantially pure form.

46. The sodium salt of 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine, said salt being in substantially pure form.

48. 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine having a purity of greater than 90% by weight.

59. 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine, in crystalline form, having a purity of greater than 90% by weight.

60. 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine, in crystalline form, having a purity of greater than 95% by weight.

61. A pharmaceutically acceptable salt of 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine.

The examiner relies on the following references:

Huber	3,624,251	Nov. 30, 1971
Slater et al. (Slater)	3,688,438	Sep. 5, 1972
Walker et al. (Walker)	3,706,181	Dec. 19, 1972
Niebylski et al. (Nieblyski)	3,790,365	Feb. 5, 1974
Verheyden et al. (Verheyden)	4,507,305	Mar. 26, 1985
Thomas et al. (Thomas)	4,565,867	Jan. 21, 1986
Knudsen	4,689,129	Aug. 25, 1987
Bell et al. (Bell)	4,714,787	Dec. 22, 1987
Hannah et al. (Hannah)	4,845,084	July 4, 1989
Ellis	4,910,035	Mar. 20, 1990
Eisner et al. (Eisner)	5,185,365	Feb. 9, 1993
Chou	5,401,861	Mar. 28, 1995

Grose, W.F.A., English Language Translation of Doctoral Thesis (1971)

Pandit et al. (Pandit), "A New Class of Nucleoside Analogues. Synthesis of N_1-pyrimidinyl- and N_9-purinyl-4'-hydroxy-3-(hydroxymethyl)butanes," Synthetic Communications, Vol. 2, No. 6, pp. 345-351 (1972)

Greene, in Protective Groups in Organic Synthesis, John Wiley & Sons, New York, pp. 29-31 (1981)

Stewart, in The Peptides, Vol.3, Academic Press, New York, pp. 180-181 (1981)

The claims stand rejected as follows:

I. Claims 32, 33, 45 and 46 under the second paragraph of 35 U.S.C. § 112.

II. Claims 33, 59, 60 and 61 under the first paragraph of 35 U.S.C. § 112 as lacking an adequate written description in the specification.

III. Claims 32, 33 and 45 under 35 U.S.C. § 102(b) as anticipated by Pandit.

IV. Claims 30, 48, 59 and 60 under 35 U.S.C. § 102(e) as anticipated by Hannah.[3]

V. Claims 30 and 48 under 35 U.S.C. § 103 as unpatentable over Pandit, Grose, Stewart, Greene and Verheyden.

DELIBERATIONS

Our deliberations in this matter have included evaluation and review of the following materials: (1) the instant specification, including all of the claims on appeal; (2) appellants' main Brief (Paper No. 51) and the Reply Brief (Paper No. 53); (3) the examiner's Answer (Paper No. 52); (4) the above-cited references relied on by the examiner; and (5) the four declarations filed under the provisions of 37 C.F.R. § 1.132: the Jarvest 1 and Harnden declarations, submitted in parent application serial no. 07/085,216 in 1988 and 1990, respectively; the Jarvest 2 declaration, executed December 17, 1992; and the Jarvest 3 declaration, executed June 3, 1998.

BACKGROUND

As indicated above (n. 2), the present application is descended, through a chain of continuing applications, from application serial no. 07/085,216, now U.S. Patent No. 5,075,445. We note that patented claim 1 is directed to "[a]n antiviral compound . . . designated 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine," also known as penciclovir or PCV, "or a pharmaceutically acceptable salt thereof, said compound being in a substantially pure, crystalline form and having a melting point of about 275°-277° C."

[3] In the Answer, the examiner states that the claims are rejected under § 102(b), as anticipated by Hannah, but this appears to be in error, see e.g., Paper No. 37.

Patented claim 2 is directed to "[t]he sodium salt of said compound of claim 1." We further note that the terminal portion of any patent granted on the present application that would extend beyond the expiration date of U.S. Patent No. 5,075,445 has been disclaimed (see the Terminal Disclaimer recorded under 37 C.F.R. § 1.321(b)/(c), Paper No. 29 of the present application).

The claims that are the subject of this appeal are also directed to 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine and certain of its salts, but they stand rejected for reasons related to the various purity limitations in the claims.

DISCUSSION

I. Indefiniteness

We begin with the proposition that "the definiteness of the language employed [in a claim] must be analyzed - - not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971).

Regarding the term "substantially pure" in claims 45 and 46, much has been said by both the examiner and appellants[4] - in our view, most of it irrelevant. The arguments of appellants and the examiner notwithstanding, the test for definiteness, first and foremost, is simply whether one skilled in the art would understand the language of the

[4] See the 4th through 14th pages of the Answer (after page 3 of the Answer, the pagination is missing or incorrect); pages 5-10 of the Brief; and pages 8-14 of the Reply Brief.

claims when the claims are read in light of the specification. See Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986).

Turning to the specification (page 5), we find the following passage to be instructive:

> [A] preferred compound of the present invention is the compound of formula (A) [9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine] or a salt or acyl derivative thereof.
>
> In a further aspect of the invention there is provided a compound of formula (A) in a purity state of greater than 60% preferably greater than 80% more preferably greater than 90% and particularly preferably more than 95% by weight of pure compound.
>
> In yet a further aspect of the invention, there is provided an isolated, substantially completely pure compound of formula (A), or a pharmaceutically acceptable salt thereof.

Thus, the specification indicates that the invention encompasses the compound, 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine, or its salt, in various states of purity: e.g., "in a purity state of greater than 60%," "greater than 80%," "greater than 90%," "more than 95% by weight of pure compound," and finally, "yet a further" level of purity - "substantially completely pure." Given this progression, we believe that one skilled in the art would understand claims 45 and 46 to require a level of purity more stringent than "more than 95% by weight of pure compound." Like the ubiquitous term "about," "the term 'substantially' is a descriptive term commonly used to 'avoid a strict numerical boundary to the specified parameter.'" Ecolab Inc. v. Envirochem Inc., 264 F.3d 1358,

1367, 60 USPQ2d 1173, 1179 (Fed. Cir. 2001), (quoting Pall Corp. v. Micron Seps., 66 F.3d 1211, 1217, 36 USPQ2d 1225, 1229 (Fed. Cir. 1995)). In our view, "substantially pure," as it appears in these claims, interpreted in light of the specification, reasonably serves to describe the claimed subject matter to those of skill in the art.

According to the examiner, the spectroscopic data in claims 32 and 33 are "of unknown function, and hence, render[ ] the claim[s] indefinite." Answer, 15th page. Having reviewed Example 4 of the specification (which describes acid hydrolysis of a precursor compound; recrystallization to yield 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine; and analysis of the recrystallization product), in conjunction with the first paragraph of the Appendix accompanying the Jarvest 3 declaration (which describes the results of a re-analysis of the recrystallized product from Example 4), it is clear that, with one exception, the only data reported in Example 4 and listed in the claims are those associated with 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine per se; data associated with the impurities in the recrystallization product are reported in the declaration, but excluded from the claims. The one exception is the negative limitation in claim 33 regarding the absence of a "substantially detectable signal in the δ 7.1-7.4 region" of the NMR spectrum. According to appellants, the absence of any signal in this region indicates that the claimed compound is free of any significant quantities of [ ] monobenzyl and dibenzyl ether contaminants." Brief, page 13. Thus, we agree with the examiner that the spectroscopic data in the claims reflect "intrinsic properties" of 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine, and do not reflect either the presence or absence of impurities (with the exception of the monobenzyl and dibenzyl ether

contaminants). Nevertheless, we do not agree that the recitations of spectroscopic properties render the claims indefinite. In our view, the recitations are merely superfluous.

Accordingly, the rejection of claims 32, 33, 45 and 46 under 35 U.S.C. § 112, second paragraph, is reversed.

II. Written Description

According to the examiner, the term "having substantially no detectable signal in the δ 7.1 - 7.4 region" in claim 33 lacks description in the specification. Answer, 18th page. The examiner states that " it is assumed that what appellants really mean is that they claim a sample which is sufficiently pure not to have any signals in that region," "even though, of course, that is not the way the claim is actually written (Id.), adding that "[i]f appellants were to submit a high resolution NMR of the material in example 4, and there were in fact no detectable signals in that region, this rejection would vanish" (Id., 19th page). Nevertheless, appellants have provided a re-analysis of the actual material produced in Example 4 of the specification (see the Appendices of the Jarvest 3 and 4 declarations), identifying the so-called "non-characterizing signals," which account for the percentage of impurities found in that sample, and none fall in the δ 7.1 - 7.4 region. While we agree with the examiner's assessment that that the data recited in claim 33 have no bearing on the overall purity of what is claimed, we believe that appellants, through Example 4, have adequate basis for the negative limitation in claim 33. Thus, the rejection of claim 33 as lacking adequate written descriptive support cannot be sustained on this basis.

According to the examiner, claims 59 and 60 lack descriptive support in the specification as "the crystalline material [is described] only in the 275-277°C melting point form, not in the 90% or 95% pure form" and "[t]here is no evidence that the 275-277°C melting point form corresponds to either of these." Answer, 20th page. The examiner concedes that "if appellants actually showed that the 275-277°C melting point form was inherently that pure, the rejection [would] vanish," but maintains that the Jarvest 3 declaration is inconclusive on this point because "it is not known whether this was in fact a crystalline form that was being analyzed" as "neither Jarvest's declaration nor the original text for example 4 state that the product actually is crystalline" and "recrystallization attempts do not always give crystalline products." Id. Appellants, however, point out that "the original text of Example 4 does not state that recrystallization 'was attempted,' but that the product 'was recrystallized.'" Brief, pages 15-16. We agree with appellants that the continued rejection of claims 59 and 60 on this basis is in error.

The examiner argues that claims 61, directed to "a pharmaceutically acceptable salt of Penciclovir without any purity limitation at all," lacks written descriptive support because "the language appears in the two earlier of the three priority documents ([but] not in the third)" and that "[l]egally, this is not sufficient[,] [d]escription must be found in the specification." Answer, 19th page. We find this argument to be without merit - we know of no authority, and the examiner cites none, that requires an ipsis verbis disclosure to satisfy the written description requirement.

Accordingly, the rejection of claims 33, 59, 60 and 61 under 35 U.S.C. § 112, first paragraph, is reversed.

III. Anticipation by Pandit

Claims 32, 33 and 45 stand rejected under 35 U.S.C. § 102(b) as anticipated by Pandit, even though the examiner concedes that "Pandit has a disclosure of Penciclovir in a form less pure than here, with more and different impurities." Answer, 20th page.

With respect to claim 45, the examiner argues that "the purity limitation 'substantially pure form' . . . is indefinite, and so could be broad enough to embrace the material of Pandit." Answer, 21st page. Inasmuch as there is no dispute that Pandit describes a material that is only 45-50% penciclovir by weight, and we have found that the term "substantially pure form" is not indefinite, but would be understood by one skilled in the art to require a level of purity more stringent than "more than 95% by weight of pure compound," Pandit cannot be said to anticipate the invention of claim 45.

With respect to claims 32 and 33, the examiner argues that these claims "have no purity limitation," inasmuch as the spectroscopic data recited in the claims merely reflect intrinsic properties of penciclovir and have nothing to do with purity. Thus, "since it is Penciclovir here and Penciclovir in Pandit, the same spectroscopic properties are present." Answer, 20th page. For the reasons given above (in the discussion of the rejection of claims 32 and 33 on the ground of indefiniteness), we agree with the examiner that the spectroscopic data in claim 32 reflects "intrinsic properties" of 9-(4-hydroxy-3-hydroxymethylbut-1-yl) guanine (penciclovir), and does not reflect either the

presence or absence of impurities. Thus, claim 32 does not recite a limitation that serves to distinguish over Pandit, and the rejection is affirmed with respect to this claim.

Claim 33, however, contains the limitation "having substantially no detectable signal in the δ 7.1 - 7.4 region." While we agree with the examiner that this negative limitation does not have a bearing on overall purity, it does reflect the absence of significant amounts of the monobenzyl and dibenzyl impurities found in Pandit's preparation, and thus serves as a limitation distinguishing over Pandit.

Accordingly, the rejection of claims 33 and 45 as anticipated by Pandit is reversed with respect to claim 45, but affirmed with respect to claim 32.

VI. Anticipation by Hannah

According to the examiner, appellants are not entitled to the benefit of their British priority documents under 35 U.S.C. § 119,[5] and therefore, claims 30, 48, 59 and 60 are anticipated by Hannah,[6] which "describes the material in crystalline form . . . with a melting point of 273° - 275°." Answer, 21st page.

Nevertheless, we agree with appellants that Hannah "is not prior art to Appellants' invention" for the reasons set forth in detail on pages 3-5 and 16 of the Reply Brief. The rejection of claims 30, 48, 59 and 60 over Hannah is reversed.

[5] GB 8322199, filed August 18, 1983; GB 8325271, filed September 21, 1984.

[6] U.S. Patent No. 4,845,084, filed January 26, 1984.

V. Obviousness

Claims 30 and 48 stand rejected under 35 U.S.C. § 103 as unpatentable over Pandit, Grose, Stewart, Greene and Verheyden.

As explained by appellants, "Pandit discloses an impure preparation of about 45-50% PCV and 50-55% monobenzyl and dibenzyl esters" which "was merely a chemical intermediate in the synthesis of a desired end product," i.e., "nucleotide analogues or novel nucleic acid models . . . constitut[ing] a new class of potential anti-mitotic or anti-viral agents." Reply Brief, page 5. Appellants emphasize that "Pandit presumes that it is the nucleotide produced by phosphorylation of the nucleoside . . . rather than the nucleoside itself, that has antiviral activity." Id.

The examiner concedes these points, but nevertheless argues essentially that one skilled in the art would have had both the motivation and the means to purify Pandit's intermediate preparation, inasmuch as Pandit's intermediate was known to contain monobenzyl and dibenzyl esters which would not be phosphorylated in subsequent steps, and "[o]ne skilled in the art of synthetic organic chemistry will naturally seek to maximize yields, and . . . to obtain the cleanest material possible" (Answer, 24th page) and the other secondary references (Stewart, Greene and Verheyden) "establish that there was known in the art a wide assortment of procedures for debenzylation of benzyl ethers" (Id., 26th page).

The examiner's rationale seems reasonable at first blush, but we find appellants' position on the matter to be more persuasive. As appellants point out, there is no indication in Pandit that the dihydroxy material is desirable in and of itself, Pandit's only interest in it is as an intermediate, and "[t]here is no indication in [Pandit] or any of the secondary references that the yield and purity of the material obtained in Pandit was unsatisfactory for use for the intended purpose, i.e., phosphorylation of the hydroxyl groups or their linkage via phosphodiester bridges to yield nucleotide analogues." Reply Brief, pages 7 and 8. We find ourselves in agreement with appellants that "there is no motivation to purify any of the intermediates[,]" (and there are many intermediates in Pandit) "[a]s long as the endproduct is sufficiently pure and produced in sufficient quantities." Id., page 6. Moreover, we note appellants argument that "[e]ven assuming that one would be motivated to purify each intermediate on the route to producing a desired endproduct, it would be highly inefficient to go to the time and expense of purifying any intermediate" from a purity of 45-50% to a purity of greater than 90% and greater than 95%, as required by claims 30 and 48, respectively. Id.

"The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992) (footnote omitted). In this case, we do not find evidence of a motivation, suggestion or teaching for modifying Pandit so as to arrive at the claimed invention.

Accordingly, the rejection of claim 30 and 48 under 35 U.S.C. § 103 is reversed.

SUMMARY

On consideration of the record, for the reasons discussed above, we reverse the rejections of the claims for indefiniteness and lack of written description. In addition, we reverse the rejections of the claims for obviousness over Pandit, Grose, Stewart, Greene and Verheyden, and for anticipation by Hannah. Regarding the rejection for anticipation by Pandit, we reverse the rejection with respect to claim 45, but affirm the rejection with respect to claim 32. As the result of our action today, claims 30, 33, 45, 46, 48, 59, 60 and 61 are free of rejection.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

	)
William F. Smith	)
Administrative Patent Judge	)
	)
	)
	) BOARD OF PATENT
Toni R. Scheiner	)
Administrative Patent Judge	) APPEALS AND

)
) INTERFERENCES
)
Donald E. Adams)
Administrative Patent Judge)

Thomas Hoxie
Novartis Corporation
Patent and Trademark Department
564 Morris Avenue
Summit, NJ 07901-1027